IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

43531

In re Application of:	:	
Gianfranco MERIZZI	:	Group Art Unit: 1654
Serial No.: 10/070,656	:	Examiner: M. Flood
Filed: March 8, 2002	:	

For: AN ANTIOXIDANT PREPARATION BASED ON PLANT EXTRACTS FOR THE TREATMENT OF CIRCULATION AND ADIPOSITY PROBLEMS

DECLARATION

I, Pier Antonio Bacci, contractual Professor in Aesthetic Surgery with the Surgery School of the University of Siena, Italy, hereby declare the following:

1. Attached is a report summarizing the results of a double blind placebo study of compositions according to the invention of the above-identified patent application. I personally supervised this study, reviewed the raw data from this study and prepared the report from that date.

2. I hereby certify that this report accurately summarizes the results of and conclusions to be drawn from the double blind study.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these were made with the knowledge that false statements made willfully are punishable by fine, imprisonment, or both a fine and imprisonment under Section 1001 of Title 18 of the United States; and further that false statements made willfully may jeopardize the validity of any patent issuing on an application in which the false statements were made.

Date

Pier Antonio Bacci
Professor in Aesthetic Surgery

10/09/04

RANDOMISED, PLACEBO CONTROLLED DOUBLE BLIND CLINICAL STUDY ON EFFICACY OF A COMPOSITION ACCORDING TO US Serial No. 10/070,656

A group of 87 patients, with age from 18 to 45 years, with a presence of cellulite for at least two years were recruited and randomised in two sub-groups and received different treatments according to the double blind method, namely:

- ► Group C (58 patients)
- ► Group B (29 patients).

The two products were formulated as follows:

Group C: *Ginkgo biloba* extract, *Melilotus* extract, *Centella* extract and *Fucus* extract, according to claim 1 of the present application, together with a *Ruscus* extract and Recaptacell™.

Group B: a product consisting of inert substances (natural fibres and soy oil) administered as a placebo.

The patients were instructed to take three capsules a day for a total of 47 days of said products.

After 47 days of treatment, 77 patients were examined with confirmation that they had taken the capsules regularly. The patients were included in the following groups:

- C: 51 individuals (of whom 26 underwent also additional instrumental evaluations)
- B: 26 individuals (of whom 14 underwent also additional instrumental evaluations).

The statistical analysis of the results was conducted through t-test for paired data.

MICROCIRCULATION EXAMINATIONS

Tests conducted using optical probe video capillaroscopy showed that patients affected by cellulite presented typical microangiopathy related to medium degree mixed capillary-venous stasis associated with the typical reduced juxta-capillary arteriole sphygmic activity.

Video capillaroscopy: baseline flow

	Group C	**Group B**
Baseline	1.73	1.76
Final	2.18	1.77
Final-baseline	0.45 (25.5%)	0.01 (0.6%)
Baseline vs. final	**P<0.001**	P>0.001

Video capillaroscopy: capillary density

	Group C	**Group B**
Baseline	0.75	0.81
Final	2.21	0.84
Final-baseline	1.46 (196%)	0.03 (3.7%)
Baseline vs. final	**P<0.001**	P>0.001

The measurements made using optical probe video capillaroscopy focused on the front part of the thigh on the vertical line, 15 cm from the saphenofemoral junction of the left leg, demonstrating that the baseline flow and capillary density increased in group C, expressing a microvasomotion effect, with increased perfusion in the various capillary-venule-venous zon-

es and consequent increased pan-zonal vascularisation. No statistically significant variation was observed in the placebo group. The direct correlation between capillary density and baseline flow appears particularly important. This is because an increase of the former without a similar increase of the latter would be due to venule-venous stasis and not to increased perfusion.

Flowmetry: resting flow

	Group C	**Group B**
Baseline	9.34	9.34
Final	23.11	9.53
Final-baseline	13.77 (147%)	0,19 (2%)
Baseline vs. final	**P<0.001**	P>0.001

Flowmetry: Tcp 02

	Group C	**Group B**
Baseline	68.71	65.48
Final	95.11	66.88
Final-baseline	26.4 (38.4%)	1.2 (2.1%)
Baseline vs. final	**P<0.001**	P>0.001

Laser Doppler tests (PF3 TS 1.5 sec with 30 mV gain) were conducted at the same time. It is noted that normally major arterial lesions are never observed in cellulite syndromes, while ramus dysrhythmia with low vasomotoin is more common. The results show significant microvessel activation response in individuals treated with the active product, as seen in the changes in vasomotion, observed in every treated individual, with increased resting flow and Tcp02. No noticeable statistical variations were found in the group of patients treated with the placebo.

The interpretation of this data is that the product is capable of significantly increasing microvascular flow and favouring arteriole contraction normalisation in a statistically significant way. Considering the overall improvement of the microcirculatory structure, we can readily deduce that these evident variations in microvascular functionality do not only refer to the "sphygmic" activity of the substances used involving the juxta-capillary arterioles, but also – and above all – to improvement and reactivation of the entire interstitial matrix metabolism and that the perivascular space, called the "periangium" where the most important tissue exchanges and the most delicate colloid-osmotic events occur.

ABDOMINAL CIRCUMFERENCE

	Group C	**Group B**
Baseline	77.54	73.61
Final	74.29	73.00
Final-baseline	-3.2 (-4.1%)	-0.61 (-0.8%)
Baseline vs. final	**P<0.001**	P>0.001

Abdominal circumference was significantly reduced in group C. The decrease in the placebo group is not statistically significant.